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Memory, Oscillations, and Coordination in a Computational Model of Layers 2/3 of Neocortex

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Synopsis

- Modeling in brain science
- Conceptual (”top-down”) theory
- A cortical layer 2/3 model
  - Modular network structure
  - Neuron and synapse models
  - Memory storage
- Model output and dynamics
- Ongoing developments
- What about coherence?

Modeling in brain science

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- Massive amounts of data available
  - Molecular, sub-cellular, neuronal, network, macroscopic levels
  - Measurement driven data acquisition
- Mechanistic understanding still largely lacking. Why?
  - Synthesis needed! Relating data from different sources and levels to a coherent picture
- Mathematical modelling and computer simulation helps to
  - Organize known data in a coherent fashion
  - Promote model driven experimentation
- Why large-scale simulations?
  - Connect cellular, synaptic and (brain-scale) network levels
- Data-driven vs theory-driven modeling

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Some theories of cortical perception/memory function

- Data → pruning of models, but no consensus

- Synfire chain paradigm
- Hebbian cell assembly theory
  - Attractor network paradigm, Ising model
- Binding by synchrony/phase locking
- Global workspace theory
- Liquid state machine theory
- ...
- All hypothetical, related
- All subject to simulation and analysis

Hebbian synapses and cell assemblies

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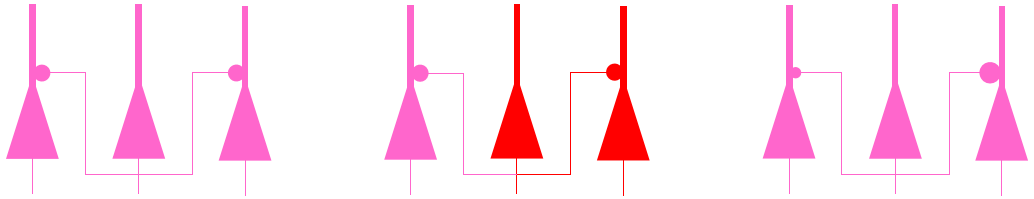
Hebb D O, 1949: The Organization of Behavior



Bliss and Lömo, 1973
Levy and Steward, 1978
LTP/LTD

- Cell assembly = mental object
- Gestalt (Holistic) perception
  - Perceptual completion
  - Figure-background segmentation
  - Perceptual rivalry
    - Milner P: + Lateral inhibition
- After activity ≈ 500 ms
  - Persistent, sustained
  - Fatigue = Adaptation, synaptic depression
- Generalizes to associative memory
  - Association chains
    - Time-asymmetric synaptic plasticity

... implemented as attractor networks

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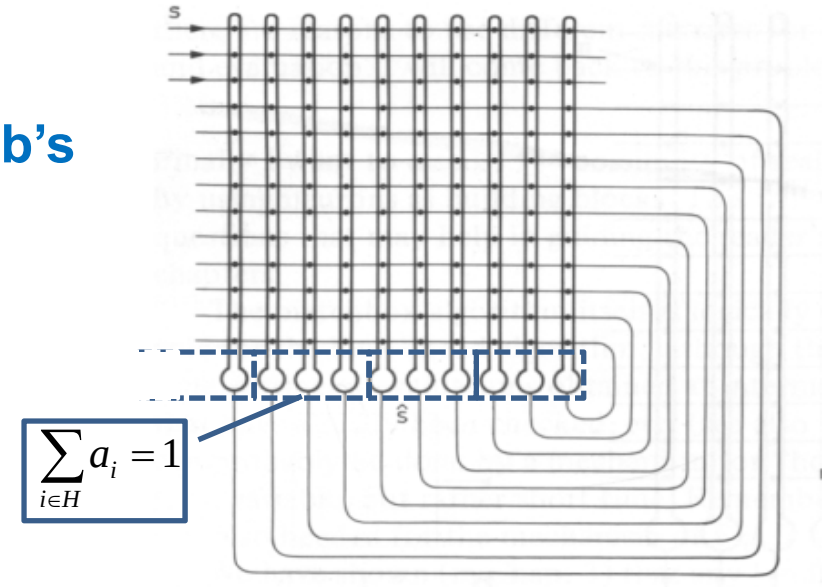
- e.g. Hopfield network
- Mathematical instanciations of Hebb's theory
- Recurrently connected
  - Layer 2/3
  - Hebbian learning rule
- Sparse
  - Connectivity
  - Activity
- Modular ("Potts network")

- Extensively studied
  - Simulations, e.g. memory properties
  - Theoretical analysis
  - Efficient content-addressable memory!



- Criticized on several points
  - Unnatural network structure
  - Dense, symmetric connectivity
  - Dense activity
  - ....

Old idea, yes
But still useful!

Support for biological plausibility

- Olfactory cortex = attractor network?
  - Haberly, Chem Senses 2001
- Hippocampus = attractor network?
  - Memory reactivation during sleep
    - Wilson and McNaughton, Science 1994
  - Attractor state like transitions
    - O'Keefe et al., Science 2005
- In vitro (local) UP-states
  - Crossart et al. 2003
- PFC, persistent activity working memory
  - Wang et al. 2001
- Recurrent cortical connectivity
  - L 2/3 & 5, higher order (association) cortex
  - Top-down projections

- Can an attractor memory be implemented by a network of real neurons and synapses?
  - Could it do some memory, perception?
  - If so, what relation to cortical functional architecture and dynamics?

Cortical computational unit(s)?

Neuron, minicolumn, hypercolumn, area, ...

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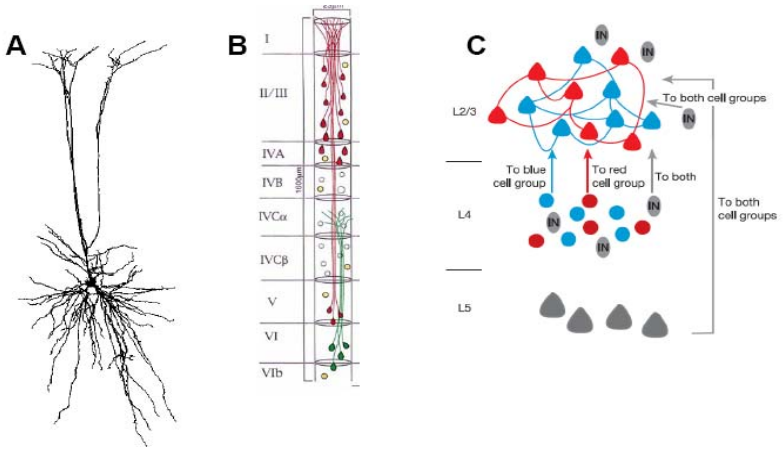
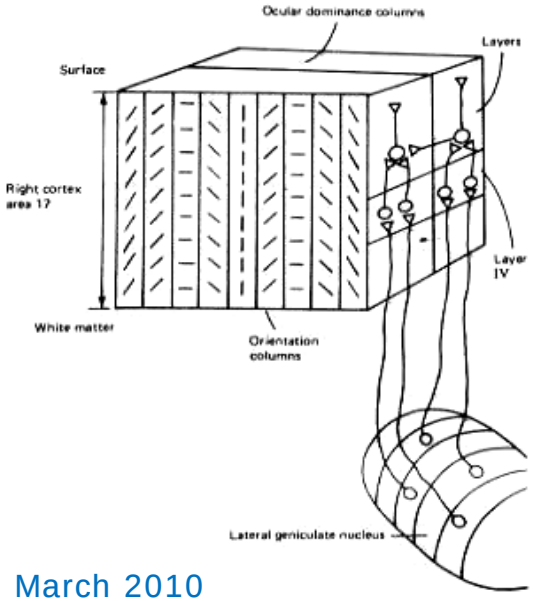
- Data on cortical connectivity, layers, columns, etc
  - From anatomy
  - From pairwise recordings
- Computational units?
  - Neuron
  - Anatomical minicolumn
  - Sub-network
  - Species/location differences?
- Hyper/Macrocolumns





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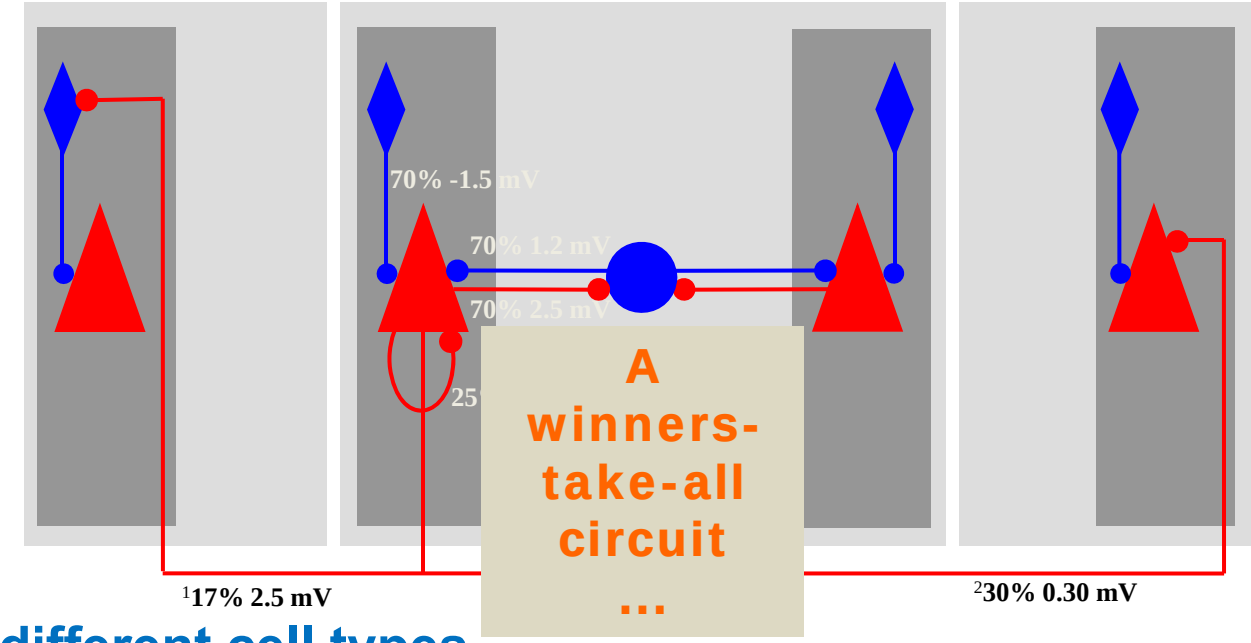
The layer 2/3 cortex model

Circuit layout



- 3 different cell types
  - Pyramidal cells, Basket cells, RSNP cells
  - RSNP = Regular Spiking Non-Pyramidal cells (dendritic targeting, vertically projecting, e.g. double bouquet cells)
- Functional minicolumns with 30 pyramidals, 2 RSNP
- Hypercolumns with minicolumns and basket cells
- (Model currently being extended with layers 4 and 5)

The layer 2/3 cortex model

Single cell model

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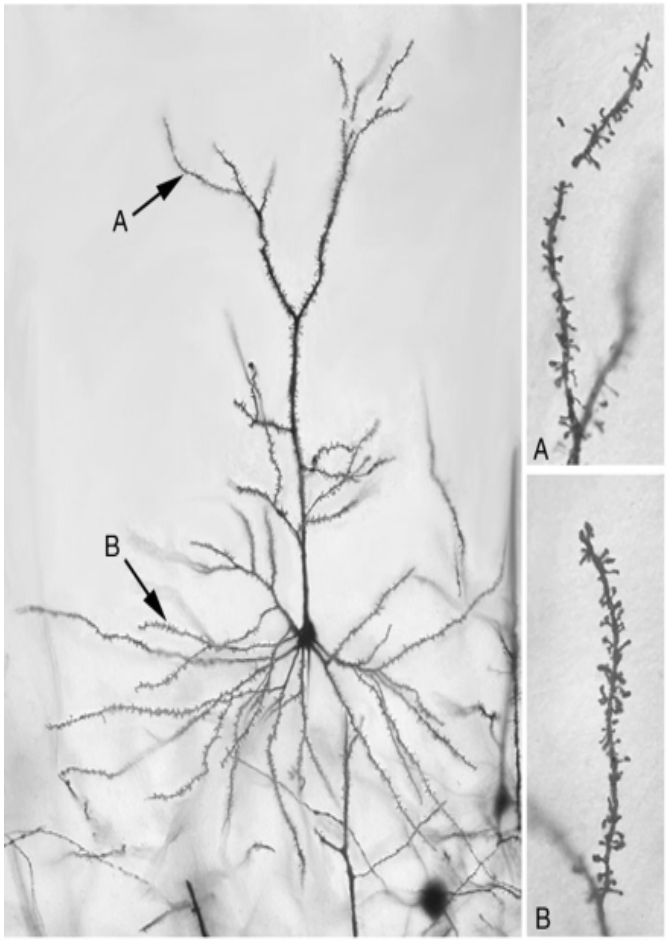

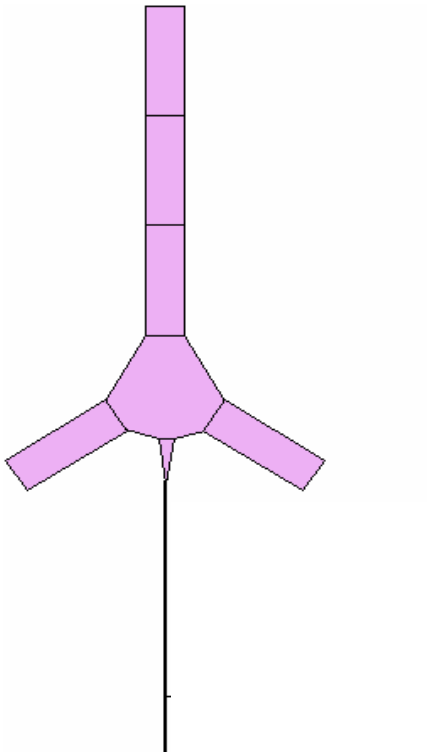

- Hodgkin-Huxley formalism
  - Na, K, K_{Ca}, Ca-channels
  - Ca_{AP} and Ca_{NMDA} pools
- Pyramidal cells
  - 6 compartments
    - IS, soma, 1 basal, 3 apikal dendritic
- Inhibitory interneurons
  - 3 compartments
    - IS, soma, dendritic
- AP and AHP shapes
- Firing properties, adaptation
- Neuron populations
  - Cell size spread (±10%)

The layer 2/3 cortex model

Synaptic properties and connectivity

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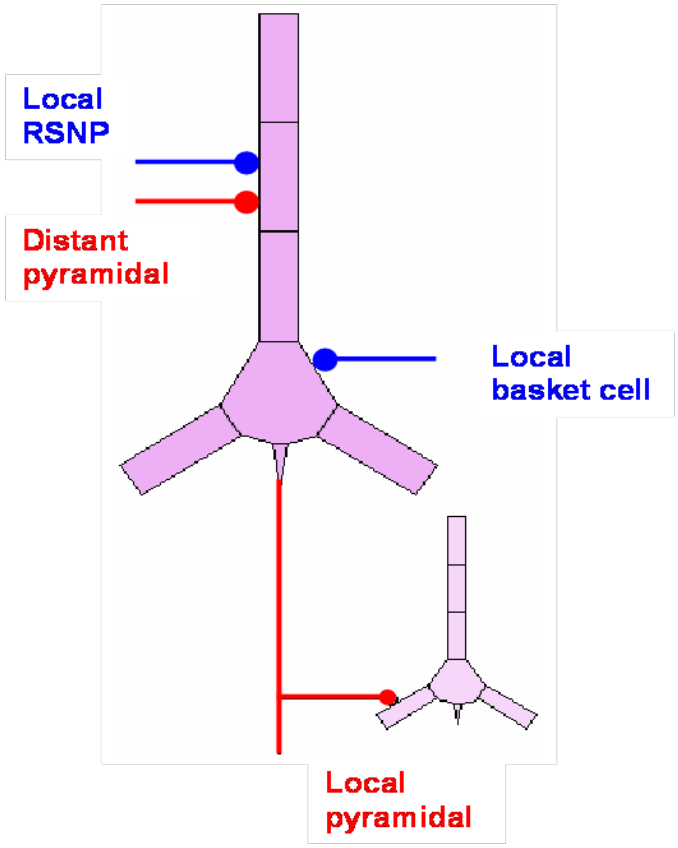

- **Synaptic transmission**
  - Glutamate (AMPA & voltage dependent NMDA)
  - Pyr-pyr synapses depressing
  - $GABA_A$
  - No gap junctions
- **Synaptic targeting of soma and dendrites**
- **3D geometry ⇒ delays**
  - 0.1 - 1m/s conduction speed
- **Realistic amplitude of PSP:s in larger network models**

Pyramidal-pyramidal fast synaptic depression
[Tsodyks, Uziel, Markram 2000]

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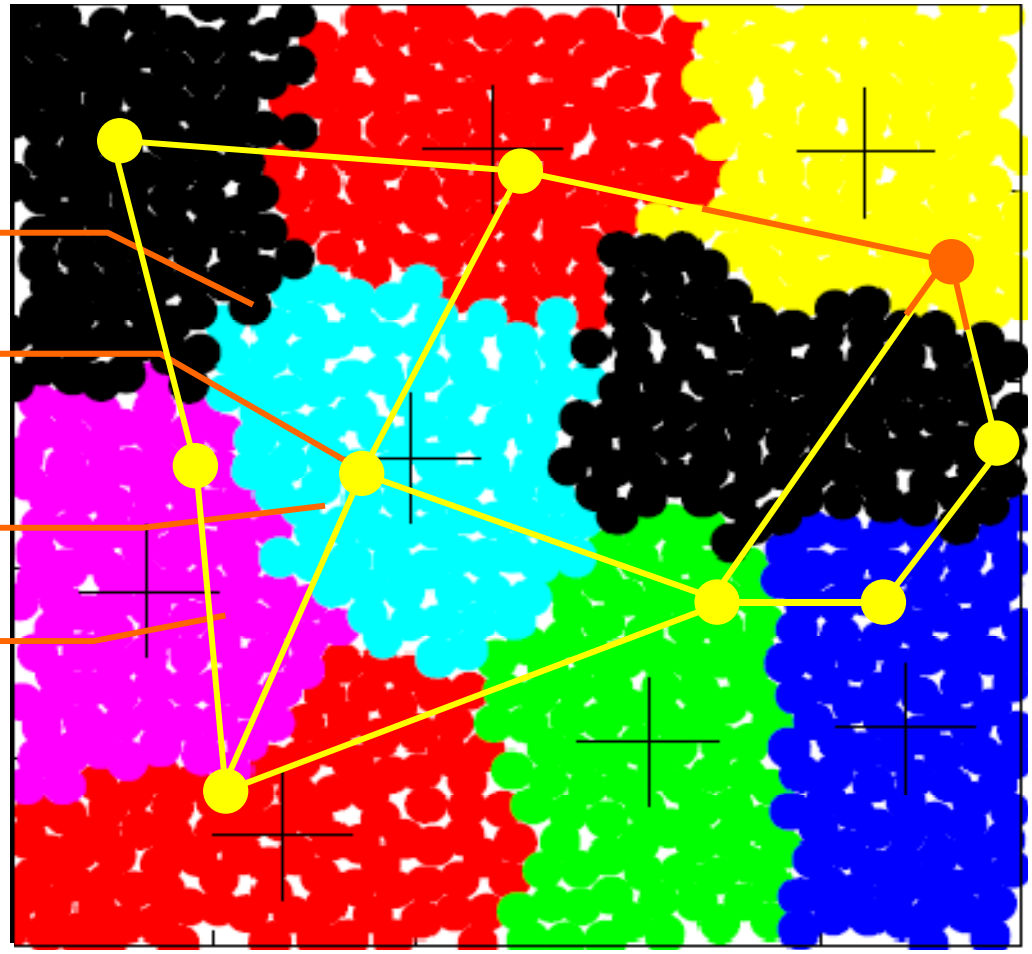
Network layout



- 1x1 mm patch
- 9 hypercolumns
- Each hypercolumn
  - 100 minicolumns
  - 100 basket cells
- 29700 neurons
- 15 million synapses
- 100 patterns stored

W created by training an isomorphic population unit network (asymmetric!)

W obeys pairwise connection statistics

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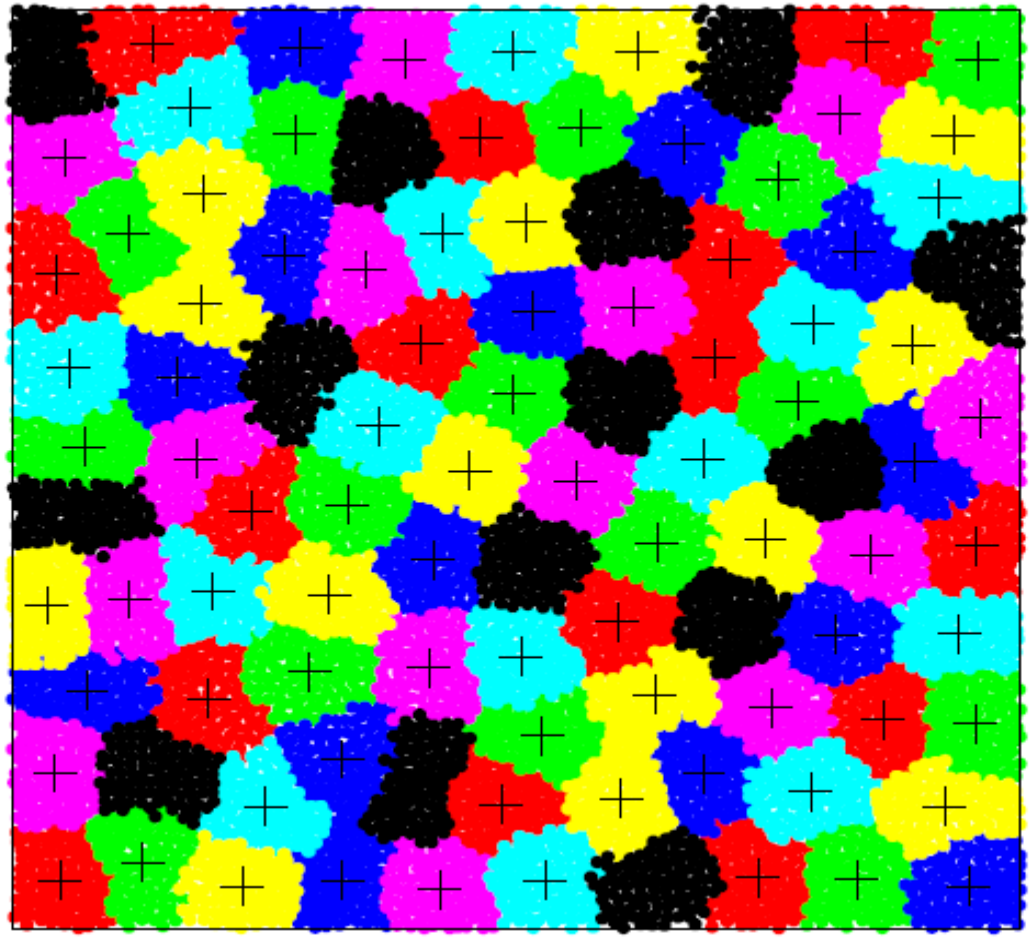
100 hypercolumns

Spontaneous activity



- 330000 neurons
- 161 million synapses

≈ 4x4 mm

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8 rack BG/L simulation

October 2006

- 22x22 mm cortical patch
  - 22 million cells, 11 billion synapses
- SPLIT simulator by KTH
- 8K nodes, co-processor mode
  - used 360 MB memory/node
- Setup time = 6927 s
- Simulation time = 1 s in 5942 s
- Massive amounts of output data
  - Network operation similar as smaller versions of the model

- 77 % estimated speedup
  - Point-point communication slows (?)
  - Linear speedup to 4K nodes

Neural simulations scale very well!
Today's largest simulations are much larger, but simpler

Djurfeldt M, Lundqvist M, Johansson C, Rehn M, Ekeberg Ö, and Lansner A (2008): Brain-scale simulation of the neocortex on the Blue Gene/L supercomputer. IBM J R&D 52:31-41

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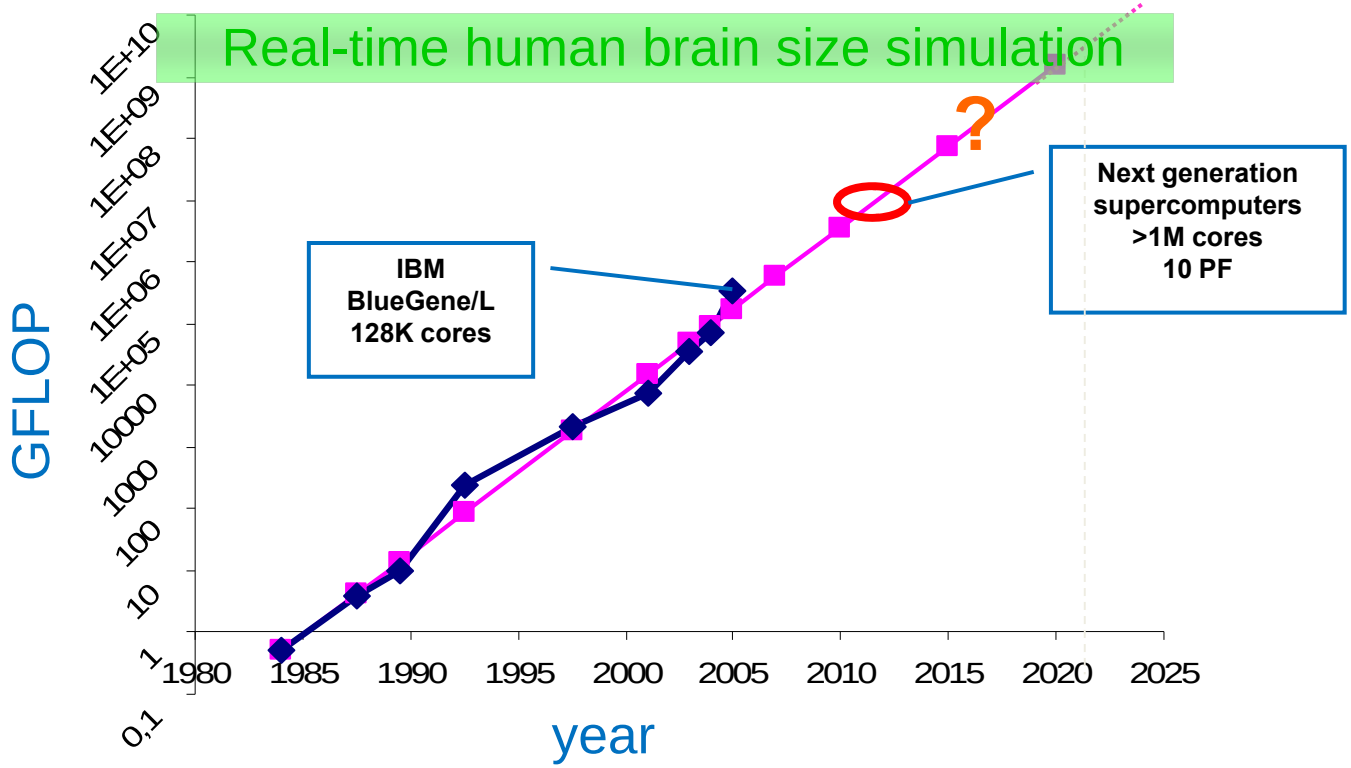
Supercomputing for brain modelling



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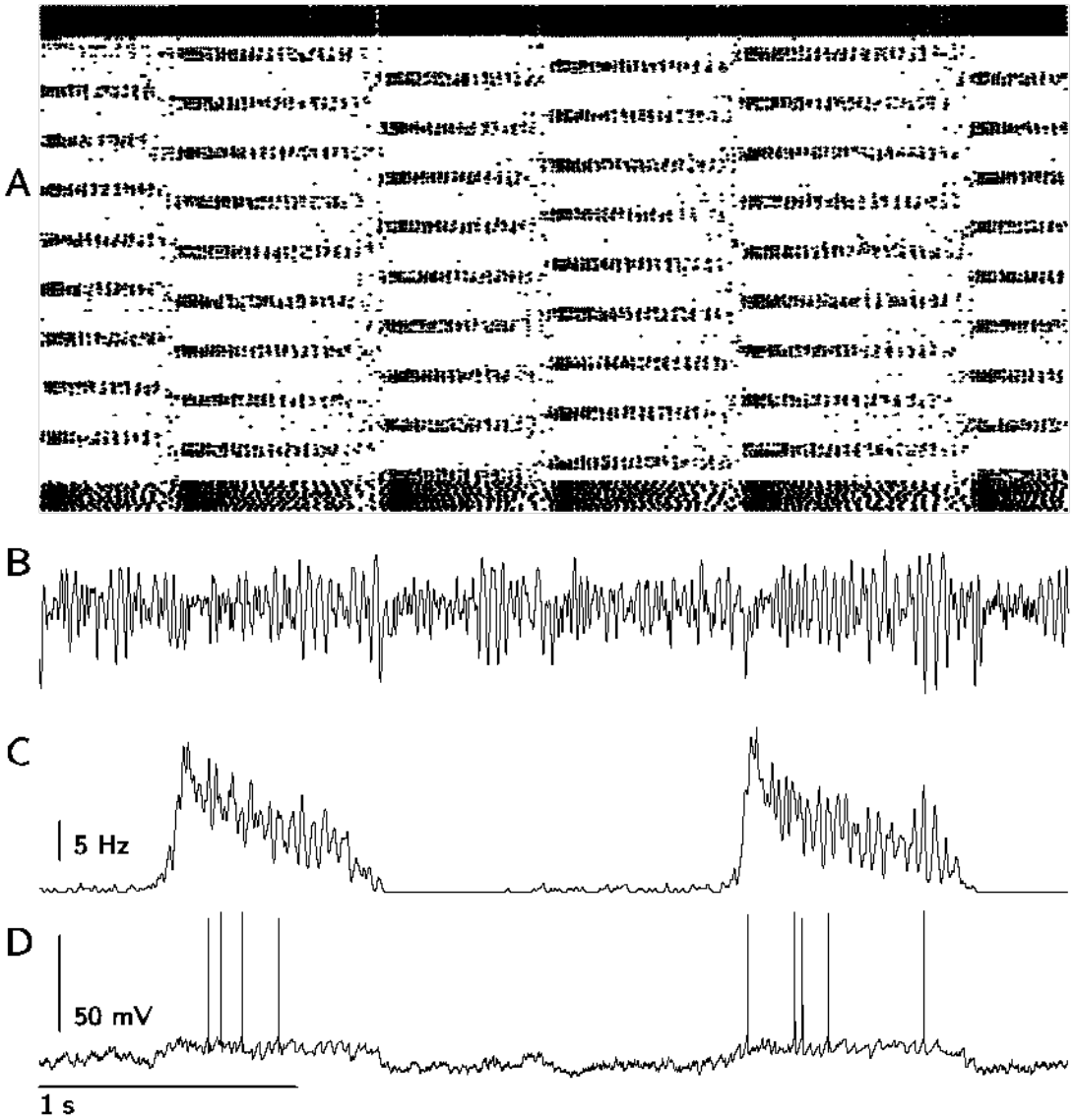
- 2000+ neurons
- 250000+ synapses
- 5 s = 600 s on PC

Spontaneous "resting activity" Tsodyks, Grinvald et al. 1999

Mishas dynamics ...

Stimulus resets!



Lundqvist M, Rehn M, Djurfeldt M and Lansner A (2006). Attractor dynamics in a modular network model of the neocortex. *Network: Computation in Neural Systems*: 17, 253-276

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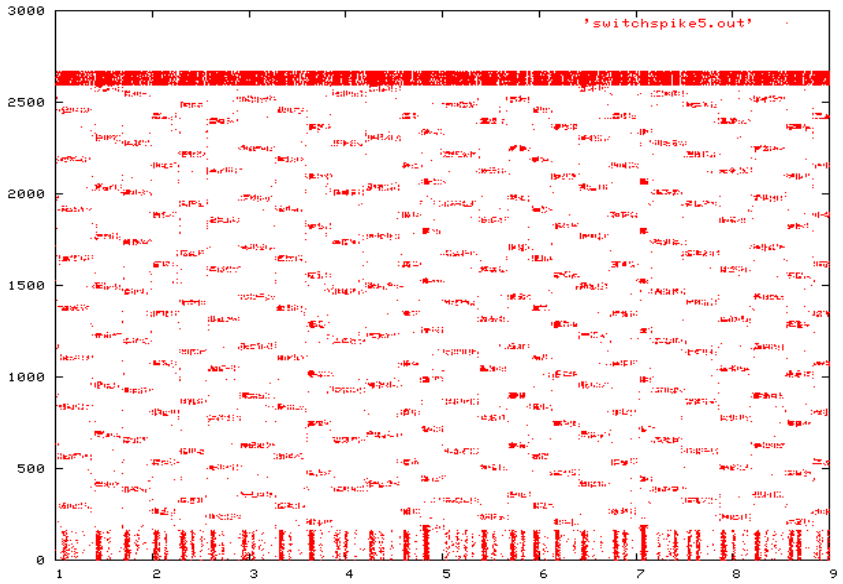
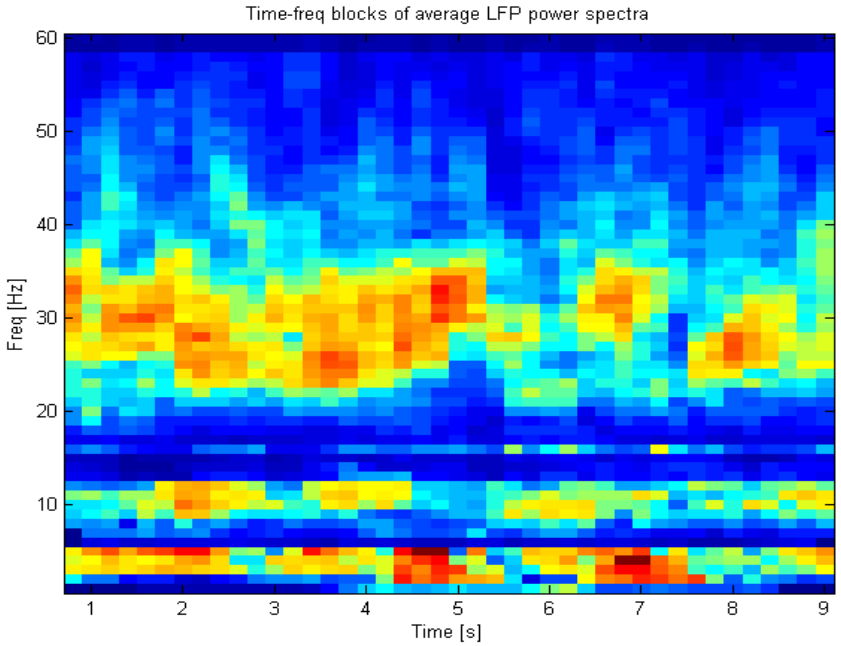
Attractor hopping



- Spike raster
  - 9 attractors



- LFP power spectrogram

Structured vs Unstructured W

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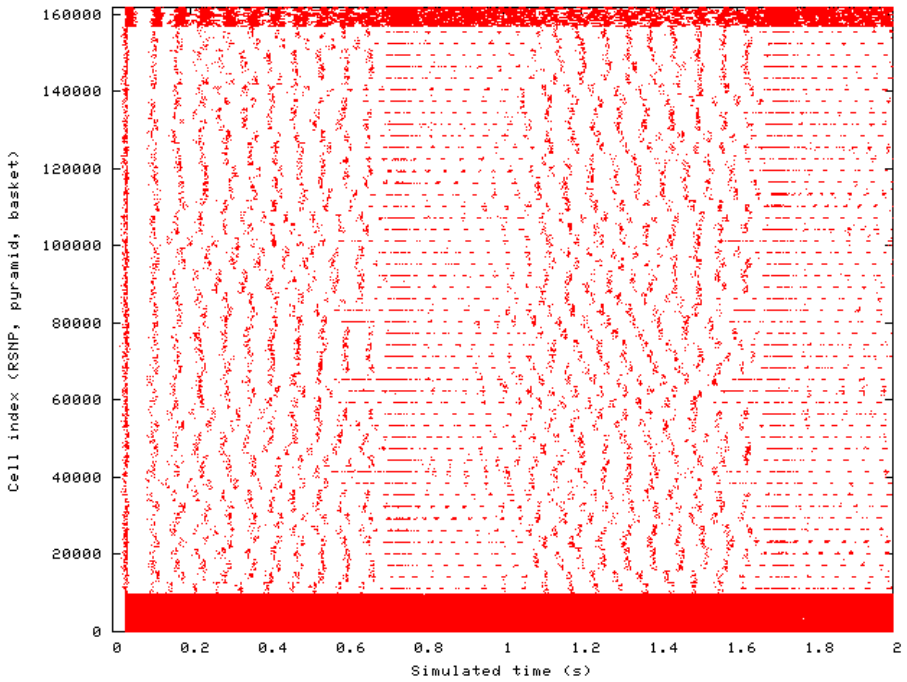

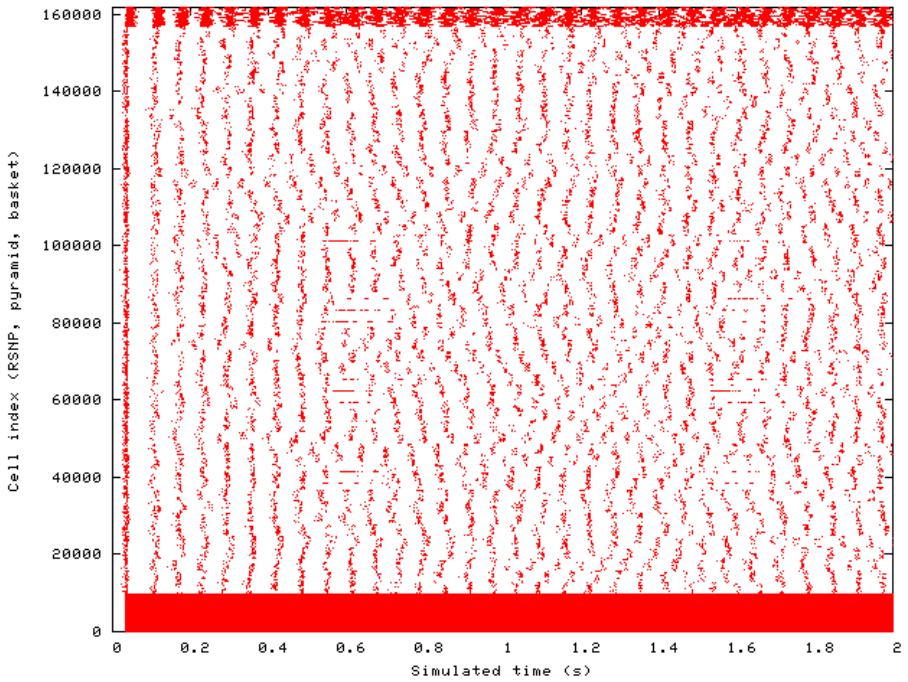

- Same cell-cell connections, but randomly permuted (right)
- Pairwise connection statistics obeyed in both cases
- NOTE: Pairwise statistics not sufficient → specific activity dependent plasticity important!

- Many E-I cortex models use random connectivity

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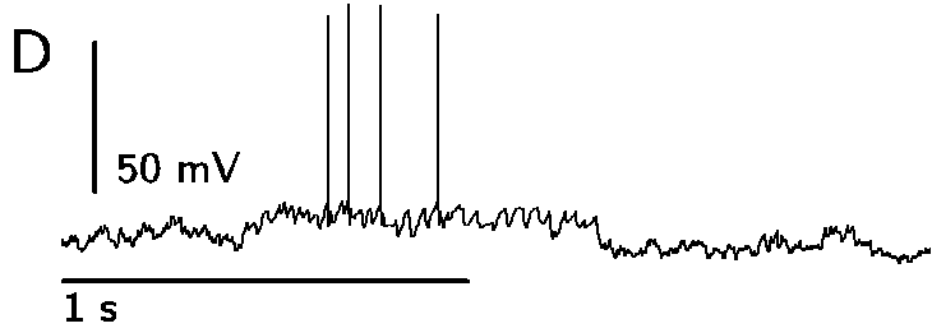
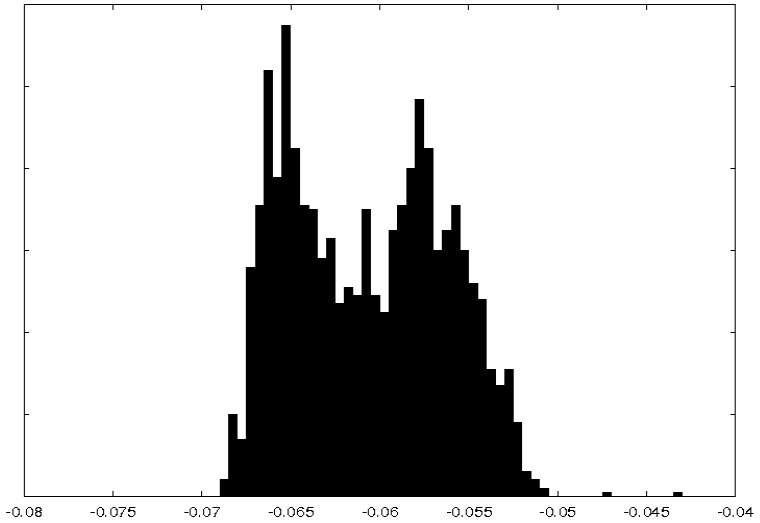
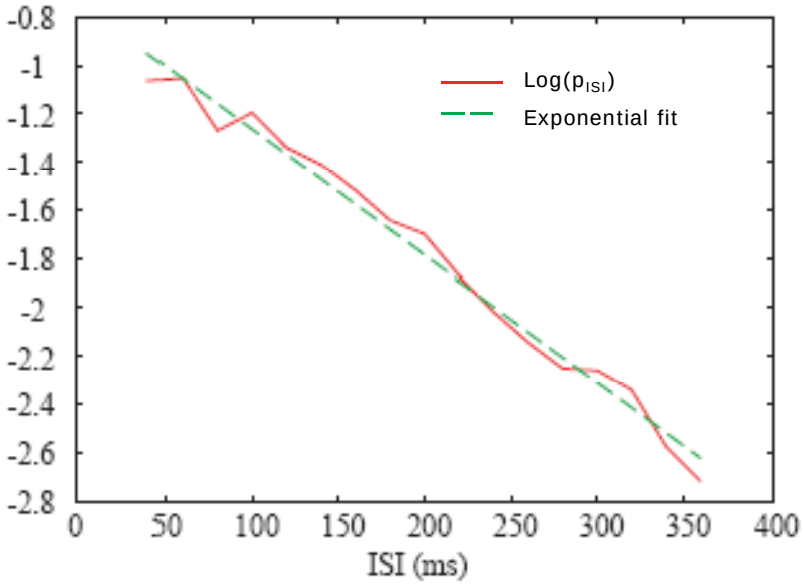
Bimodal V_m







Jeffrey Anderson, Ilan Lampl, Iva Reichova, Matteo Carandini, and David Ferster. Stimulus dependence of two-state fluctuations of membrane potential in cat visual cortex. *Nat. Neurosci.,* 3(6):617–621, 2000.

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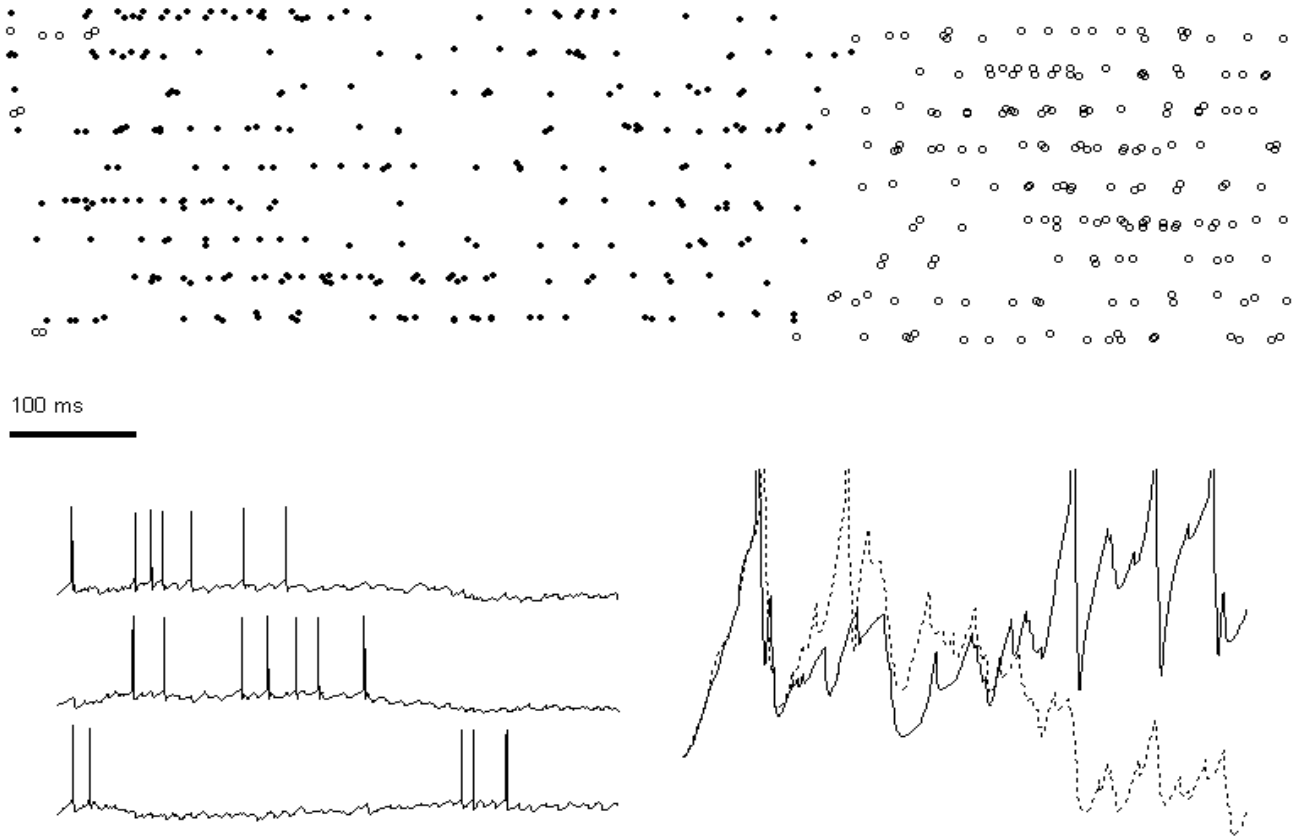
Attractor dynamics

Pattern rivalry, fast ”decision”



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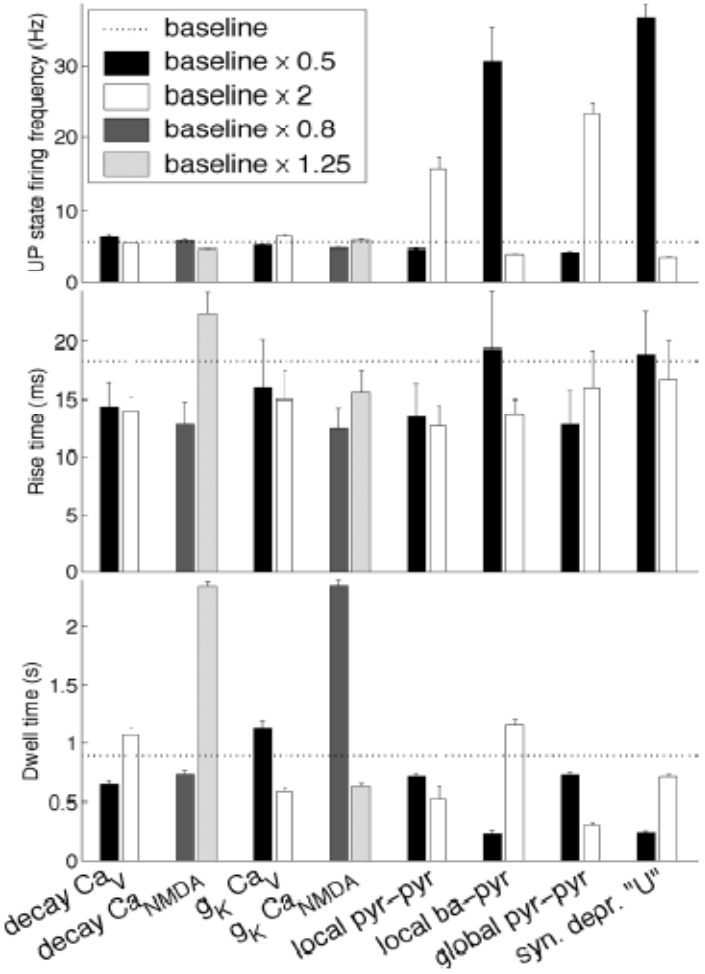
Parameter sensitivity of active state



- Each parameter ×2 and ×0.5
  - though ×1.25 and ×0.8 for slow Ca dynamics
    - or attractor states were found never to terminate
- The qualitative behavior of the system is quite robust to parameter changes
  - Most sensitive to slow Ca dynamics
- Tests by pharmacological manipulation?

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Biological plausibility of Hebbian cell assembly/attractor network model?

- Pattern reconstruction
  - Figure-background
  - Pattern completion
  - Pattern rivalry
  - 50 – 100 ms settling time
- Persistent after-activity
  - 150 ms – 2 sec
  - $NMDA_{Ca}$, K_{Ca} modulation
- Attentional blink model
- Operation robust to parameter changes and scaling

- Replicates oscillatory field potentials and spiking patterns seen *in vivo*

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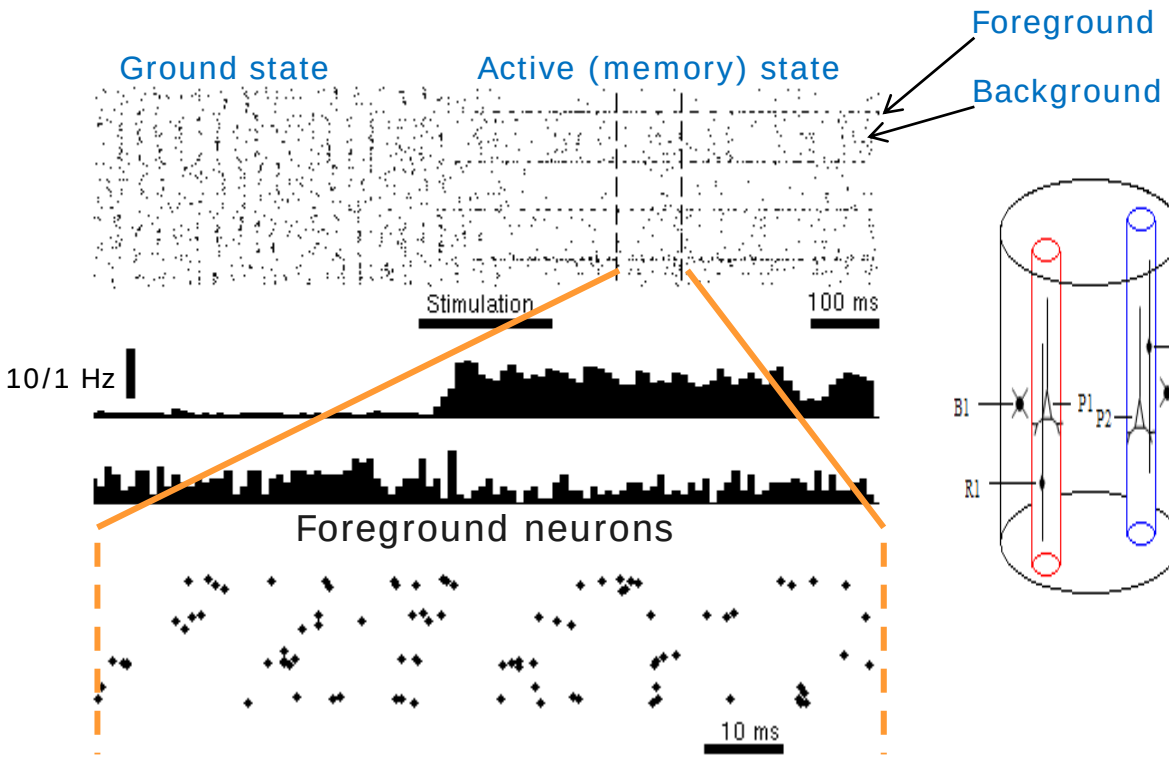
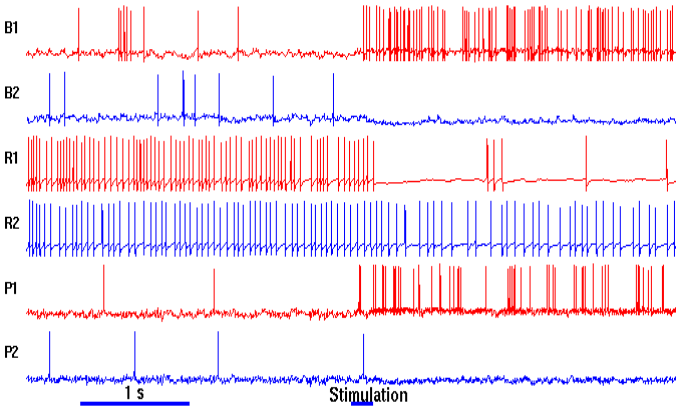
Bistable, irregular firing, spike synchronization





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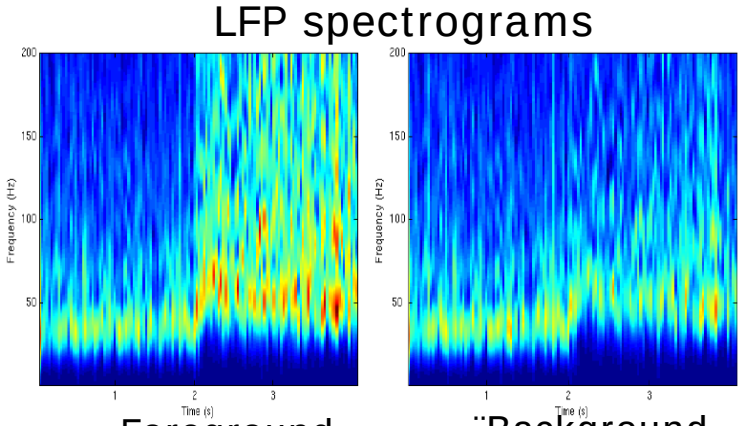
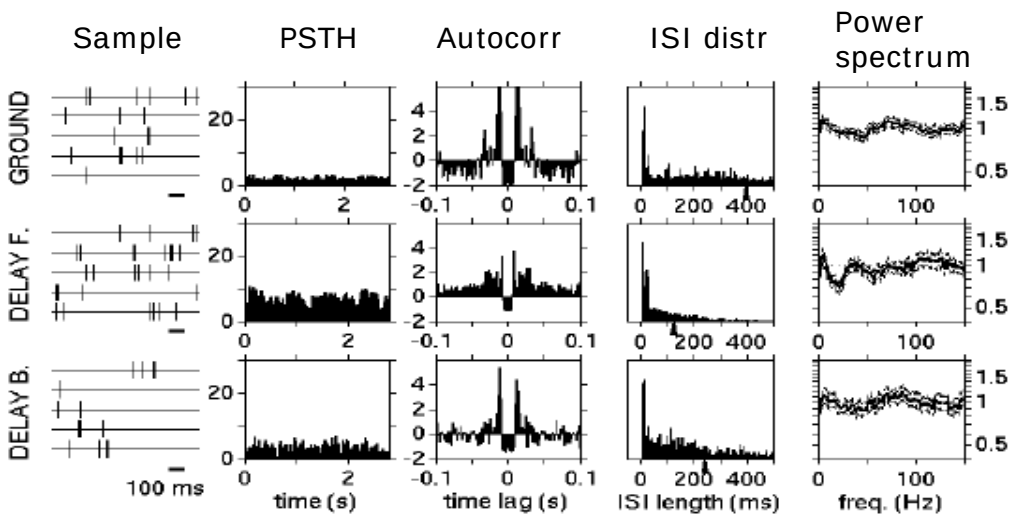
Bistable, irregular firing, spike synchronization cont'd

- Pyr↔Bc gamma oscillator
- Balanced excitation-inhibition/ inhibition dominated
- LFP oscillations
  - ground state (20-40 Hz)
  - active state (40-60 Hz)
  - not detectable at single cell level (spikes)
- Spiking activity comparable to experimental data
  - Joelving et al. 2007
  - Rudolph M, et al. 2007





Pyramidal cells

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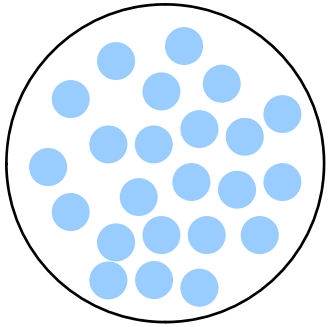
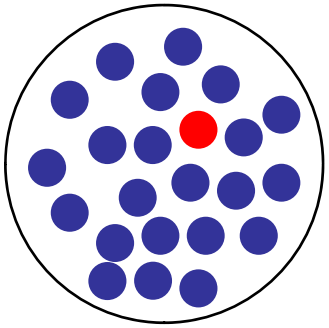
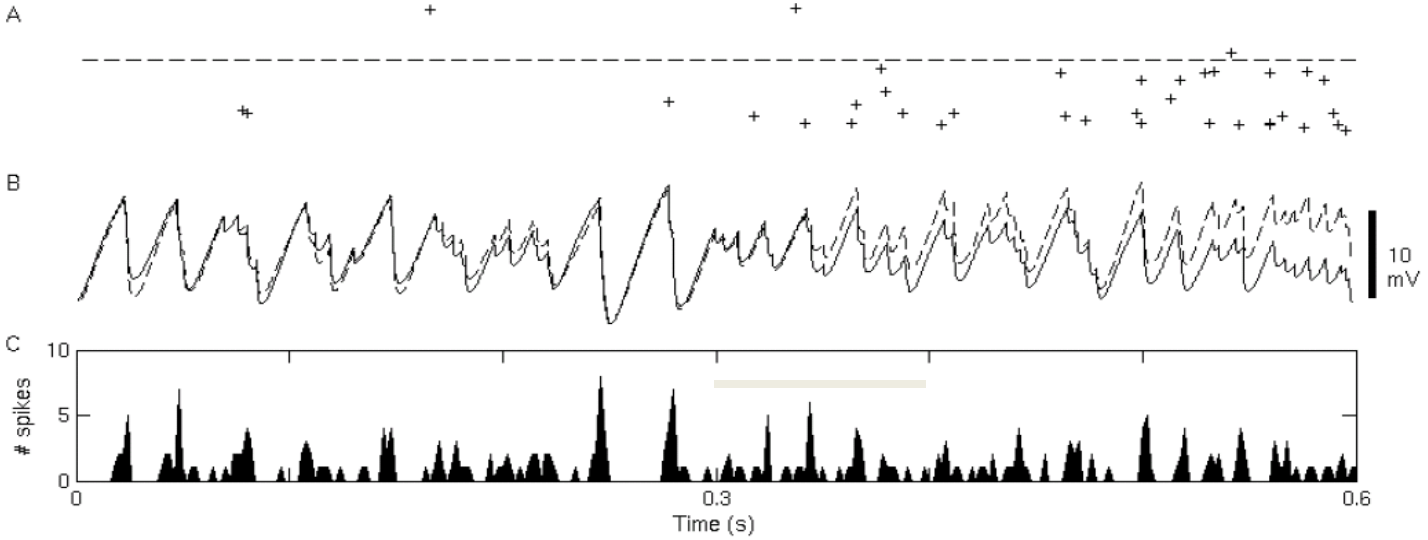
Spiking activity
in ground and active state

- Ground state – diffuse
- Active state – focused
- V_m is oscillatory
  - Foreground neurons lead
- N:o spikes same in ground and active states







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Oscillations and irregular spiking

- First attractor memory model to show population oscillations in both ground and active state
  - Beta (?) in ground state
  - Gamma in active state
- ... and low rate irregular spiking of neurons
- Characteristics of *in vivo* cortical activity

- Why is this model different?
  - RSNP inhibitory interneuron? No ...
  - Modularity - hypercolumns and minicolumns?

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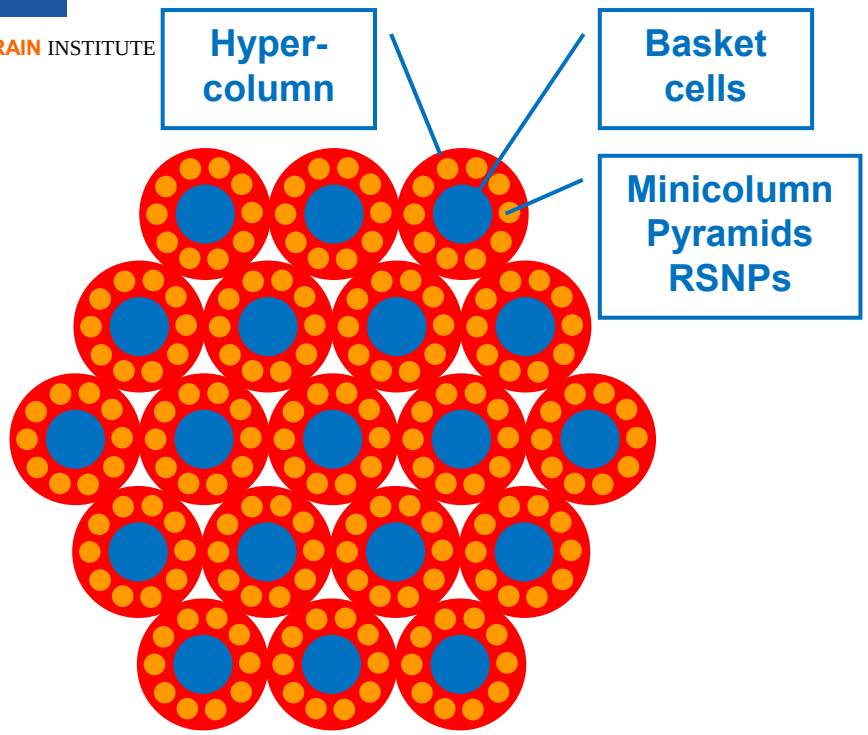
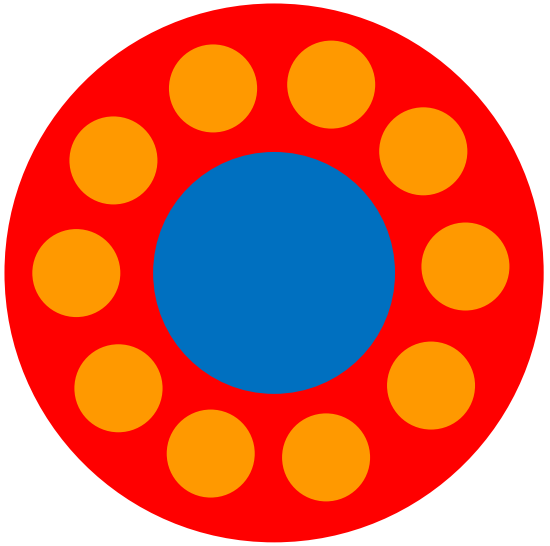
Importance of modularity





Hypercolumns – local inhibition

Stable persistent activity
Local gamma & spike synchrony
Global asynchrony

No modules – global inhibition

Unstable persistent activity
Global gamma & spike synchrony

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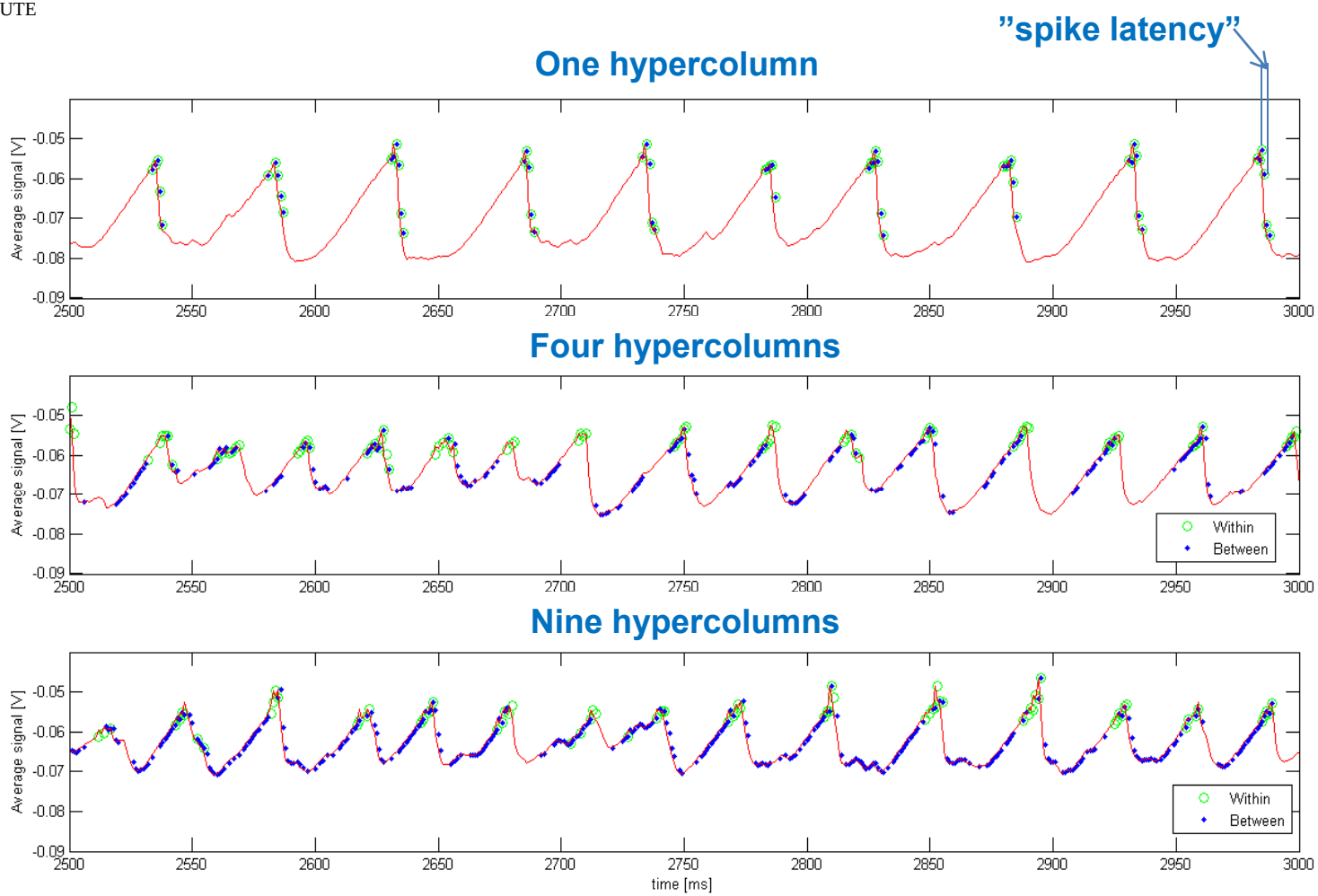
Average V_m and spikes* in one minicolumn



* from pyramidal cells

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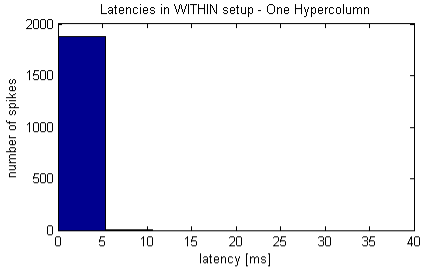
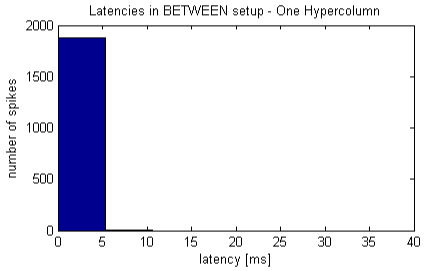
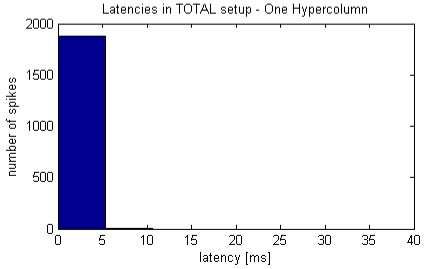
V_m – spike latency histograms

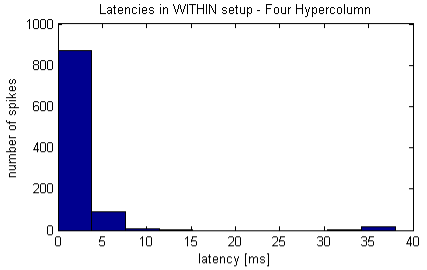
One hypercolumn

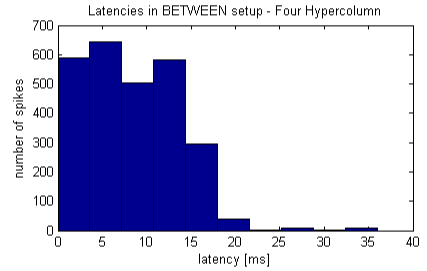


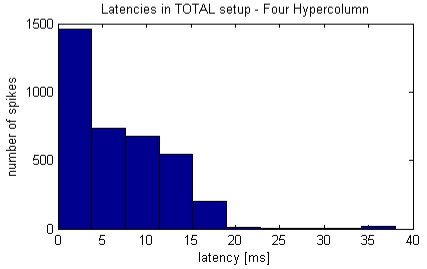




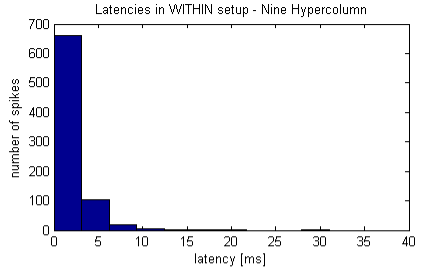
Four hypercolumns

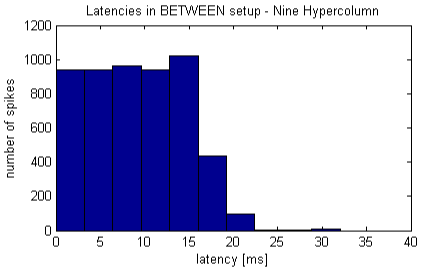


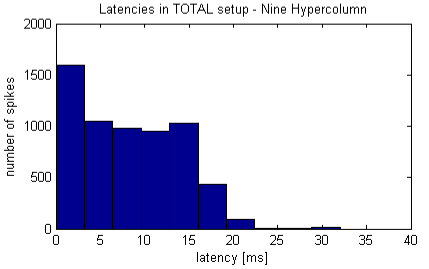




Nine hypercolumns







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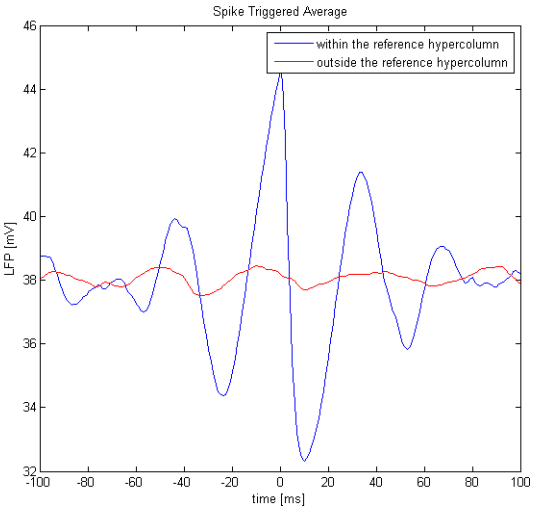
Importance of modular network structure

- Modular structure – hypercolumns, minicolumns
- Basket cell inhibition local to a hypercolum
- The E-I network of the hypercolumn – source of gamma oscillations
- Gamma synchrony
  - High within module
  - Low between modules
- Non-synchronous spikes contribute to stability of active states



Next steps

- More complex, brain-scale multi-area cortical models
- Long-range cortico-cortical connectivity
  - Feed-forward, lateral, feedback (”top-down”) projections
  - Self-organization, sparse connectivity
  - Learning, localist representations
- Multi-modal integration
- Interacting memory systems, WM ... LTM
- Attentional modulation, effects of task relevance
- Matching to multiple measurements
  - Synthesis of macroscopic measurements
    - LFP, EEG, VSD, Ca-imaging, BOLD, ...
  - Coherence, synchronization, ...

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What about coherence?

- Quasistable attractors – lower dimensional manifold, multi-stability
  - Dynamic [perceptual] decision
  - Spontaneous/Stimulus driven activity
  - EEG Microstates = ?
- Spatial extent
  - Synchrony at lower frequencies (attractor hopping)
  - Coupled areas/attractors, large-scale cortex models
- Temporal coordination
  - Overlapping, chained, nested, attractors ...
  - Richer spatio-temporal dynamics

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